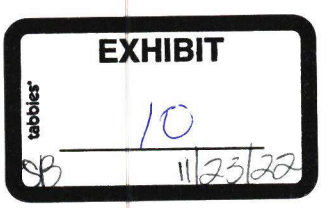
## References


1. Wan, Y., Shang, J., Graham, R., Baric, R. S. & Li, F. Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS. *J. Virol.* (2020) doi:10.1128/JVI.00127-20.
2. Letko, M. & Munster, V. Functional assessment of cell entry and receptor usage for lineage B β-coronaviruses, including 2019-nCoV. *bioRxiv* 2020.01.22.915660 (2020) doi:10.1101/2020.01.22.915660.
3. Hoffmann, M. *et al.* The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. *bioRxiv* 2020.01.31.929042 (2020) doi:10.1101/2020.01.31.929042.
4. Sheahan, T. *et al.* Mechanisms of zoonotic severe acute respiratory syndrome coronavirus host range expansion in human airway epithelium. *J. Virol.* **82**, 2274–2285 (2008).
5. Cui, J., Li, F. & Shi, Z.-L. Origin and evolution of pathogenic coronaviruses. *Nat. Rev. Microbiol.* **17**, 181–192 (2019).
6. Follis, K. E., York, J. & Nunberg, J. H. Furin cleavage of the SARS coronavirus spike glycoprotein enhances cell-cell fusion but does not affect virion entry. *Virology* **350**, 358–369 (2006).
7. Longping, V. T., Hamilton, A. M., Friling, T. & Whittaker, G. R. A novel activation mechanism of avian influenza virus H9N2 by furin. *J. Virol.* **88**, 1673–1683 (2014).
8. Alexander, D. J. & Brown, I. H. History of highly pathogenic avian influenza. *Rev. Sci. Tech.* **28**, 19–38 (2009).
9. Luczo, J. M. *et al.* Evolution of high pathogenicity of H5 avian influenza virus: haemagglutinin cleavage site selection of reverse-genetics mutants during passage in chickens. *Sci. Rep.* **8**, 11518 (2018).
10. Menachery, V. D. *et al.* A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. *Nat. Med.* **21**, 1508–1513 (2015).
11. Ge, X.-Y. *et al.* Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature* **503**, 535–538 (2013).
12. Hu, B. *et al.* Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLoS Pathog.* **13**, e1006698 (2017).
13. Zeng, L.-P. *et al.* Bat Severe Acute Respiratory Syndrome-Like Coronavirus WIV1 Encodes an Extra Accessory Protein, ORFX, Involved in Modulation of the Host Immune Response. *J. Virol.* **90**, 6573–6582 (2016).
14. Yang, X.-L. *et al.* Isolation and Characterization of a Novel Bat Coronavirus Closely Related to the Direct Progenitor of Severe Acute Respiratory Syndrome Coronavirus. *J. Virol.* **90**, 3253–3256 (2015).

**From:** Jeremy Farrar
**Sent:** Tue, 4 Feb 2020 20:26:23 +0000
**To:** Collins, Francis (NIH/OD) [E];Fauci, Anthony (NIH/NIAID) [E]
**Subject:** Re: Prevalence of infection and stage of the epidemic in Wuhan

Wild West.....

---

**From:** Francis Collins (b) (6)
**Date:** Tuesday, 4 February 2020 at 20:23
**To:** Jeremy Farrar (b) (6), "Fauci, Anthony (NIH/NIAID) [E]" (b) (6)
**Subject:** RE: Prevalence of infection and stage of the epidemic in Wuhan

Surely that wouldn't be done in a BSL-2 lab?

**From:** Jeremy Farrar (b) (6)
**Sent:** Tuesday, February 4, 2020 9:03 AM
**To:** Fauci, Anthony (NIH/NIAID) [E] <(b) (6) Collins, Francis (NIH/OD) [E] <(b) (6)
**Subject:** Re: Prevalence of infection and stage of the epidemic in Wuhan

Exactly!

---

**From:** "Fauci, Anthony (NIH/NIAID) [E]" (b) (6)>
**Date:** Tuesday, 4 February 2020 at 13:18
**To:** Francis Collins (b) (6), Jeremy Farrar (b) (6)
**Subject:** RE: Prevalence of infection and stage of the epidemic in Wuhan

?? Serial passage in ACE2-transgenic mice

**Anthony S. Fauci, MD**
**Director**
**National Institute of Allergy and Infectious Diseases**
**Building 31, Room 7A-03**
**31 Center Drive, MSC 2520**
**National Institutes of Health**
**Bethesda, MD 20892-2520**
**Phone:** (b) (6)
**FAX: (301) 496-4409**
**E-mail:** (b) (6)

**From:** Collins, Francis (NIH/OD) [E] (b) (6)
**Sent:** Tuesday, February 4, 2020 6:12 AM
**To:** Jeremy Farrar (b) (6)
**Cc:** Fauci, Anthony (NIH/NIAID) [E] (b) (6)
**Subject:** RE: Prevalence of infection and stage of the epidemic in Wuhan

Yes, I'd be interested in the proposal of accidental lab passage in animals (which ones?).

Francis

**From:** Jeremy Farrar (b) (6)
**Sent:** Tuesday, February 4, 2020 6:08 AM
**To:** Collins, Francis (NIH/OD) [E] (b) (6)
**Cc:** Fauci, Anthony (NIH/NIAID) [E] (b) (6)
**Subject:** Re: Prevalence of infection and stage of the epidemic in Wuhan

Being very careful in the morning wording

"Engineered" probably not.

Remains very real possibility of accidental lab passage in animals to give glycans. Will forward immediately or if you want to give Eddie a ring.

Eddie would be 60:40 lab side. I remain 50:50...

On 4 Feb 2020, at 10:58, Collins, Francis (NIH/OD) [E] (b) (6) wrote:

Very thoughtful analysis. I note that Eddie is now arguing against the idea that this is the product of intentional human engineering. But repeated tissue culture passage is still an option – though it doesn't explain the O-linked glycans.

Francis

**From:** Jeremy Farrar (b) (6)
**Sent:** Tuesday, February 4, 2020 2:01 AM
**To:** Fauci, Anthony (NIH/NIAID) [E] (b) (6)>; Collins, Francis (NIH/OD) [E] (b) (6)
**Subject:** FW: Prevalence of infection and stage of the epidemic in Wuhan

Please treat in confidence – a very rough first draft from Eddie and team – they will send on the edited, cleaner version later.

Pushing WHO again today